

**REMARKS**

In the present Amendment, claim 1 has been amended to incorporate the recitation of claim 7, and claim 7 has been canceled, accordingly. In addition, the phrase "or a polyphosphoric acid or a salt thereof" has been moved within the claim to clarify the claim language.

Claim 9 has been amended to clarify that it depends solely from claim 1, and is not a multiple dependent claim.

Non-elected claims 11-13 have been canceled, without prejudice or disclaimer.

New claims 14 and 15 have been added.

Claim 14 depends from claim 1, and recites that the carrier for cell culture is brought into contact with the compound of formula (I) for a period of from 5 minutes to 2 hours to effect the removal treatment.

Claim 15 also depends from claim 1, and recites that the compound of formula (I) is 1-hydroxyethane-1,1-diphosphoric acid (HEDP). Support for claims 14 and 15 may be found in the present specification at page 15, lines 7-9 and at page 20, line 1, respectively.

Upon entry of the amendments, which is respectfully requested, claims 1-6, 8-10 and 14-15 will be pending.

At page 2 of the Action, the Abstract is objected to for using phrases such as "such as" and "the like".

In response, appropriate corrections have been made to the Abstract.

Reconsideration and withdrawal of the objection to the Abstract are requested.

Also at page 2 of the Action, claim 9 is objected to because of the informality noted in the last paragraph on page 2 of the Action.

In response, an appropriate correction to claim 9 has been made.

Reconsideration and withdrawal of the objection to claim 9 are respectfully requested.

At page 3 of the Action, claim 1 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

As explained at page 3 of the Action, the Examiner expresses the view that the punctuation used in claim 1 renders it indefinite.

In response, Applicants have relocated the phrase "or a polyphosphoric acid or a salt thereof" within the claim, as noted above. This amendment is believed to address the Examiner's concern.

In view of the above, the Examiner is respectfully requested to reconsider and withdraw the §112, second paragraph, indefiniteness rejection of claim 1.

At page 4 of the Action, claims 1-6 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent 6,821,107 to Hara et al, in view of U.S. Patent 5,292,525 to Brenden et al.

Specifically with respect to independent claim 1, the Examiner states that Hara teaches a method for detaching cells from a carrier having an alginate gel layer, by bringing the carrier into contact with a chelating agent to solubilize the alginate gel layer. The Examiner states that Hara teaches solubilizing the alginate gel layer with chelating agents that include polyaminocarboxylic

acids, such as EDTA, and oxycarboxylic acids, and teaches that the chelating agent can be appropriately selected according to the multivalent metal ion of the alginate gel.

The Examiner concedes that Hara does not teach a compound of formula (I), as recited in Applicants' claim 1.

However, the Examiner states that Brenden teaches a method of removing an alignate from a cutaneous substrate by adding a composition containing a chelating polyphosphate, such as sodium hexametaphosphate. The Examiner asserts that Brenden teaches that polyphosphate chelating agents are preferred because of their lower toxicity. The Examiner states that sodium hexametaphosphate is an exemplified chelating agent of the present invention (see pages 20 and 21 of the specification).

The Examiner reasons that it would have been *prima facie* obvious to replace the chelating agent in the method of Hara, with the chelating agent of Brenden, which is stated to be a chelating agent of Applicants' formula (I). The Examiner believes that one of ordinary skill in the art would have been motivated to perform the method of Hara with the chelating agent of Brenden with a reasonable expectation of success, because Brenden allegedly teaches that polyphosphate chelating agents are less toxic and can effectively remove alginate from cutaneous substrates.

Applicants submit that this rejection should be withdrawn because Hara and Brenden do not disclose or render obvious the method for detaching a carrier for a cell culture from cultured cells formed on the surface of the carrier, of the present invention.

In the present Amendment, the recitation of claim 7 has been incorporated into independent claim 1. Claim 7 was not subject to this rejection.

The presently claimed compounds of formula (I) successfully avoid the decomposition in aqueous solution and maintain high ability of solubilization of an alginic acid gel by the introduction of a hydrocarbonic linking group as L<sup>11</sup>. Such is not taught by Brenden.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the §103 rejection of claims 1-6 based on Hara in view of Brenden.

At page 10 of the Action, claims 1-10 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent 6,821,107 to Hara et al, in view of Esser et al, *Frensenius J. Anal. Chem.* (2000).

The Examiner concedes that Hara does not teach a chelating agent of Applicants' Formula (I), (II), or (III).

However, the Examiner states that Esser teaches the chelating agents of Hara (e.g. EDTA) and those of Applicants' formulas (I), (II), and (III).

The Examiner reasons that it would have been *prima facie* obvious to replace the chelating agent in the method of Hara, with other chelating agents of Esser. The Examiner believes that one of ordinary skill in the art would have been motivated to perform the method of Hara with other chelating agents taught by Esser with a reasonable expectation of success, because Esser allegedly teaches that these chelating agents are functional equivalents in terms of their chelating properties.

AMENDMENT UNDER 37 C.F.R. §1.111  
U.S. Appln. No. 10/690,568

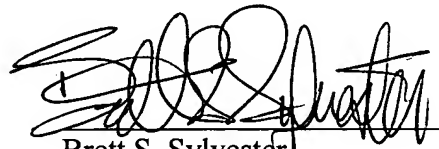
Applicants submit that this rejection should be withdrawn because Hara and Esser do not disclose or render obvious the method of the present invention.

A *prima facie* case of obviousness has not and cannot be established based on Hara and Esser. In this regard, Esser does not teach the solubilization of alginic gels with the chelating agents disclosed therein, and appears to only teach the copper chelating property of these agents. Esser does not teach that the compounds disclosed therein are equivalent for solubilizing an alginate gel having a cultured cell formed thereon. Esser only teaches copper-chelating properties. Thus, there is no reason why a person of ordinary skill in the art would have been motivated to perform the method of Hara with other chelating agents taught by Esser, with a reasonable expectation of success.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the §103 rejection of claims 1-10 based on Hara in view of Esser.

Allowance is respectfully requested.

Respectfully submitted,



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